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MCDERMOTT, WILL & EMERY
4370 LA JOLLA VILLAGE DRIVE, SUITE 700
SAN DIEGO, CA 92122

EXAMINER

PONNALURI, PADMASHRI

ART UNIT PAPER NUMBER

1639

DATE MAILED: 09/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/839,469

Applicant(s)

HUSE ET AL

Examiner

Padmashri Ponnaluri

Art Unit

1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 May 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 and 39-47 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 39-47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The response filed on 5/16/05 has been fully considered and entered into the application.
2. Claim 39 has been amended by the amendment filed on 5/16/05. Claims 1-9 and 39-47 are currently pending and are being examined in this application.

Withdrawn Claim Rejections

3. The rejections of claims 1-9, 39-47 under 35 USC. 112, second paragraph have been withdrawn in view of the amendment to the claim 39 and applicants response.
4. The new matter rejection of claims 5 and 43 has been withdrawn in view of applicant's response.

Maintained Claim Rejections

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
6. The written description rejection of claims 1-9, 39-47 has been maintained for the reasons set forth in the previous office action mailed on 11/16/04.
7. Claims 1-8, 39-46 are rejected under 35 USC. 102 (b) as being anticipated by US Patent 5,426,856 (Lerner) for the reasons set forth in the previous office action mailed on 11/16/04.
8. Claims 1-5, 8-9, 39-43 and 46-47 are rejected under 35 USC 102 (e) as being anticipated by US Patent 6,287,787 B1 (Houghten) for the reasons set forth in the previous office action mailed on 11/16/04.

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9. Claims 1, 6-7, 9, 39 and 46-45, 47 are rejected under 35 USC 102 (e) as being anticipated by US Patent 5,912,335 (Bergsma et al) for the reasons set forth in the previous office action mailed on 11/16/04.

10. Claims 1-9, 39-47 are rejected under 35 USC 103(a) as being unpatentable over US Patent 5,912,335 (Bergsma et al) and US Patent 5,844,094 (Hudson et al) for the reasons set forth in the previous office action mailed on 11/16/04.

Response to Arguments

11. Applicant's arguments filed on 5/16/05, regarding the written description rejection, have been fully considered but they are not persuasive.

Claims 1-9, 39-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is written description rejection.

The instant claims briefly recite a method for determining binding of a receptor to one or more ligands comprising contacting a collective receptor variant population with said one or more ligands and detecting binding of said one or more ligands to said collective receptor variant population.

To satisfy the written description requirement, an applicant may convey reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

The instant specification discloses that 'receptor' is capable of selectively binding to a ligand, and is generally macromolecules such as polypeptides, nucleic acids, carbohydrates or lipid; 'ligand' refers to a molecule selectively bind to a receptor, and the ligand can be any type of molecule such as polypeptide, nucleic acid, carbohydrate, lipid or any organic derived compound; and the further the specification discloses ligand can be a receptor and conversely, a molecule that is a receptor can also be a ligand since ligands and receptors are defined

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*as binding partners. The specification discloses that the 'variant' is molecule that shares **similar** structure and function; and 'optimal binding' characteristics will depend on the particular application of the binding molecule.*

The specification example discloses that the parent receptor is a mouse monoclonal antibody, and six variant receptors were generated and screened for binding to anti-idiotypic antibody ligands. The specification has no other examples of ligands, receptors or variants of receptors. The specification has not disclosed methods in which the receptor variant population is divided into subpopulations. The specification discloses hypothetical methods, in which the receptor variant population can be screened by dividing ligand population into subpopulations or individual ligands to determine the binding activity [see 0016]. The specification has not disclosed oligonucleotide or carbohydrate or lipid or organic molecule as 'ligand' or 'receptor.' The specification discloses general methods for expressing the receptor variants in melanophore cells (example I). The specification has not disclosed the receptor variant which binds to a ligand identified by the claimed method. The specification discloses general methods of identifying a receptor sequence which specifically binds to a ligand, and methods of generating variants of the receptor recombinantly, and methods of screening for the variant.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials. \equiv University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (1997), quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in University of California v. Eli Lilly defined the invention by function of the claimed DNA (encoding insulin)].

Thus, it requires a representative sample of compounds (i.e., receptor, ligand) or a showing of sufficient characteristics to demonstrate possession of the claimed invention.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention (see MPEP 2163).

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The instant specification discloses general hypothetical methods in which binding partners can be identified. The specification has no working examples other than the mouse monoclonal antibody variants and anti-idiotypic antibody which binds to it as ligands and receptors.

An applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. See, e.g., Vas-Cath, 935 F.2d at 1565, 19 USPQ2d at 1118.

In the present instance, the claimed invention contains no identifying characteristics regarding the receptors, ligands or the receptor variant, except the generic definitions. The variant receptors have to be prepared and further screened to identify the variant, which binds to the ligand, thus the variants have to be prepared. The specification has not disclosed which peptides, polynucleotides, carbohydrates, or organic molecules have the 'optimal binding activity', and in absence of teachings in the specification the claimed method can not be said to have been described adequately.

Applicants assert that applicants have complied with the written description requirement for this molecular biology invention by a mode adequate to show applicant was in possession of the invention at the time the application was filed. Applicants argue that 'unlike Lilly, applicants has not claimed a receptor, ligand or receptor variant population. Rather applicant has claimed a method and it the method has been adequately described.

Applicants argue that the written description rejection is applicable only to the compounds/ or products (see the response filed on 5/16/05, page 7, second paragraph) not to the methods. Applicant's assertions and arguments are not persuasive.

Written description requirement of 35 USC. 112 exists independently of enablement requirement, and the requirement applies whether or not case involves question of priority, since requirement applies to all inventions including chemical inventions, and since the fact that

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patent is directed to method entailing use of compound, rather than to compound per se, does not remove patentee's obligation to provide description of compound sufficient to distinguish infringing methods from non-infringing methods. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 USPQ2d 1886, 1890-93 (Fed. Cir.2004).

Thus, according to University of Rochester, the written description requirement is applicable to method claims, not only just products/compounds as in applicant's arguments.

Applicants further argue that 'an adequate description of the method of the invention does not require a detailed description of the ligand, receptor or receptor variant because any of the molecules or classes of molecules described in the application are sufficient with only a general knowledge of its structure.

Applicant's arguments have considered and are not persuasive. The specification discloses general definitions of a receptor, ligand which are applicable to any molecule and further hypothetical methods of screening for the receptors. The claimed methods are drawn to the use of a genus of ligands and/or receptors.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

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The limited specification example discloses mouse monoclonal antibodies (receptor) and methods of generating and screening variants of the antibodies for binding to the ligands, which is not a representative of the claimed method of screening for any receptor variant using any ligand.

Thus, the written description rejection of record has been maintained for the reasons set forth in the previous office action mailed on 11/16/04.

12. Applicant's arguments filed on 5/16/05 regarding the anticipatory rejections of claims 1-9, 39-47 have been fully considered but they are not persuasive.

NOTE that the response filed on 5/16/05 has addressed different anticipatory rejections over Lerner et al, Houghten et al, and Bergsma et al together.

a. *Claims 1-8, 39-46 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 5,426,856 (Lerner et al).*

The instant claims briefly recite a method for determining binding of a receptor to one or more ligands comprising contacting a collective receptor variant population with said one or more ligands and detecting binding of said one or more ligands to said collective receptor variant population.

In the claims the terms 'ligand' and 'receptor' are considered as binding partners, and the further the ligand can be a receptor and conversely, a molecule that is a receptor can also be a ligand since ligands and receptors are defined as binding partners in the specification.

Lerner et al disclose a method for identifying a chemical that acts as an agonist for G protein coupled cell surface receptor (i.e., see abstract). The method uses expression of the receptors in pigment cells, specifically melanophores (i.e., see column 13, lines 54-67, example 6) (refers to instant claim recombinantly expressed in melanophores). Lerner et al discloses a multiplicity of GPC receptors that are expressed (i.e., see column 14, lines 31-49, column 15). The reference clearly teaches cloning of new GPC receptors (refers to receptor variant population of the instant claims). Lerner et al teach a variety of bioassays that can be used to screen the GPC receptors for binding to ligands (i.e., see examples 1-5) (refers to the instant claimed method). The reference also

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teaches a method for isolating a clone for a GPC receptor via a fractionation procedure (i.e., see columns 18-19). The reference specifically discloses a procedure in which colonies are tested, then subdivided into smaller pools based on positive results where each sub set is retested until a single clone is identified (refers to instant claim dividing the population into sub-populations and repeating the dividing and detecting). Thus, the reference clearly anticipates the claimed invention.

b. *Claims 1-5, 8-9, 39-43, 46-47 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,287,787 B1 (Houghten et al, filing date November 24, 1993).*

The instant claims briefly recite a method for determining binding of a receptor to one or more ligands comprising contacting a collective receptor variant population with said one or more ligands and detecting binding of said one or more ligands to said collective receptor variant population.

In the claims the terms 'ligand' and 'receptor' are considered as binding partners, and the further the ligand can be a receptor and conversely, a molecule that is a receptor can also be a ligand since ligands and receptors are defined as binding partners in the specification.

Houghten et al teach dimeric oligopeptide mixture sets (refers to the receptor variants or sub-population of receptor variants of the instant claims). Houghten discloses a library of dimeric oligopeptide mixture sets that comprise a plurality of sets of dimeric oligomer mixtures (i.e., see column 8). The reference teaches each set of the library has same length, position of mercapto residue in the chain, and each set in the library differs from the other sets by the position of one or more predetermined amino acid residue, or the identity of one or more predetermined amino acid residue (refers to the variant receptor population of the instant claims) (i.e., see column 8). The reference discloses a process for determining the sequence of a dimeric oligopeptide ligand (considered as receptor) that preferentially binds to an acceptor (considered as ligand). The method comprises a library of dimeric oligopeptide sets is admixed with an acceptor, and the binding of each set exhibiting preferential binding relative to the other set is determined, thereby identifying the amino acid sequence of the ligand (i.e., see column 8) (refers to the instant claimed method). The reference discloses that the method is repeated with each set of library. The reference teaches that the individual library sets exhibit preferential binding compared to the library used immediately before (refers to the instant claim 'optimal binding activity') (i.e., see column 9). The reference discloses that the dimeric oligopeptide mixture set to include either a radio active label or a photoreactive label

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(refers to instant claim identifiable tag) (i.e. see column 24). The reference discloses 190 dimer mixture sets, and screening those 190 sets using a binding assay. Houghten et al further disclose positional scanning assay, in which six groups of precursors molecules prepared, and each group also contained 19 different sub-group mixtures of oligopeptides, and each sub-group mixture within each group members of the group form six libraries of dimeric oligopeptide mixtures (refers to instant claim dividing said collective receptor variant population) (i.e., see example 6). The reference clearly anticipates the claimed invention.

c. *Claims 1, 6-7, 9, 39, 44-45, 47 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 5,912,335 (Bergsma et al, filing date October 03, 1996).*

The instant claims briefly recite a method for determining binding of a receptor to one or more ligands comprising contacting a collective receptor variant population with said one or more ligands and detecting binding of said one or more ligands to said collective receptor variant population.

In the claims the terms 'ligand' and 'receptor' are considered as binding partners, and the further the ligand can be a receptor and conversely, a molecule that is a receptor can also be a ligand since ligands and receptors are defined as binding partners in the specification.

Bergsma et al teach novel human G-protein coupled receptors, referred as HUVCT36 polypeptides, variants, and process of making the polypeptides. Bergsma et al teach methods of screening for compounds which bind to and activate or inhibit activation of the receptor polypeptides of the invention. The reference teaches that the 'variant polypeptides' include polypeptides which differ in amino acid sequence from another, reference polypeptide (refers to the receptor variant of the instant claims) (i.e., see column 10); and 'binding molecules' refer to molecules, including ligands that specifically bind to or interact with receptor polypeptides of the present invention (refers to the ligands of the instant claims) (I.e., see column 11). Bergsma et al teach polynucleotide encoding amino acid sequence of HUVCT36 set out in FIGS. 1A, 1B and 1c; variants, analogs, derivatives and fragments (refers to the population of receptor variant population of the instant claims). The reference teaches that vectors which include polynucleotides, which encode HUVCT36 and variants, and host cells which are genetically engineered with vectors of the invention and production of polypeptides of the invention by recombinant techniques (refers to 'recombinantly expressed in cells' of the instant claims) (i.e., see column 18). The reference teaches variety

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expression vectors to be used with the invention (i.e., see column 19). The reference teaches that the vectors generally include selectable markers.

Bergsma et al teach HUVCT36 binding molecules and assays to identify the binding molecules to HUVCT36 (i.e., see columns 29-31). The reference teaches that HUVCT36 receptor expressed in a mammalian or eukaryotic and/or yeast cells and used to screen complex biological mixtures, compound banks, and combinatorial peptide and/or organic libraries for natural and surrogate ligands, which are agonistic, and/or antagonists. In one embodiment the reference teaches that method for screening of peptide libraries for binding partners. Recombinant tagged or labeled HUVCT36 is used to select peptides from a peptide or phosphopeptide library, which interact with HUVCT36. And further the reference teaches one screening procedure includes the use of melanophores (refers to instant claims 'recombinantly expressed in melanophores') which are transfected to express the HUVCT36 of the invention to screen for test compound to observe binding, stimulation and inhibition of the functional aspect (i.e., see column 31). The reference clearly anticipates the claimed invention.

Applicants argue that none of the cited references describe 'contacting a collective receptor variant population with one or more ligands. Because none of the cited reference describe all elements of the claimed invention, neither Lerner et al, Houghten et al or Bergsma et al can anticipate the invention as claimed.

Applicant's arguments have been considered and are not persuasive. Lerner et al, Houghten et al and Bergsma et al anticipate the claimed invention for the reasons of the record.

Lerner et al teach G protein coupled cell surface receptors (refer to the receptor variants) and teaches a variety of bioassays that can be used to screen the GPC receptors for binding to ligands (which refers to the claimed method).

Houghten et al teach dimeric oligopeptide mixture (refers to the claimed receptor variants) and screening the mixture for a dimeric oligopeptide sequence which preferentially

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binds to an acceptor (refers to the ligand). Thus, Houghten et al method anticipates the claimed method.

Bergsma et al teach novel human G-protein coupled receptors (refers to the collective receptor variants of the instant claims) and methods of screening of peptide libraries (collective receptor variants) for binding partners (ligands). Thus, the reference methods anticipate the claimed methods.

Thus, the rejections of record have been maintained for the reasons set forth in the previous office action mailed on 11/16/04.

13. Applicant's arguments filed on 5/16/04 regarding the obviousness rejection of claims, have been fully considered but they are not persuasive.

Claims 1-9, 39-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,912,335 (Bergsma et al) and US patent 5,844,094 (Hudson et al).

The instant claims briefly recite a method for determining binding of a receptor to one or more ligands comprising contacting a collective receptor variant population with said one or more ligands and detecting binding of said one or more ligands to said collective receptor variant population.

In the claims the terms 'ligand' and 'receptor' are considered as binding partners, and the further the ligand can be a receptor and conversely, a molecule that is a receptor can also be a ligand since ligands and receptors are defined as binding partners in the specification.

Bergsma et al teach novel human G-protein coupled receptors, referred as HUVCT36 polypeptides, variants, and process of making the polypeptides. Bergsma et al teach methods of screening for compounds which bind to and activate or inhibit activation of the receptor polypeptides of the invention. The reference teaches that the 'variant polypeptides' include polypeptides which differ in amino acid sequence from another, reference polypeptide (refers to the receptor variant of the instant claims) (i.e., see column 10); and 'binding molecules' refer to molecules, including ligands that specifically bind to or interact with receptor polypeptides of the present invention (refers to the ligands of the instant claims) (I.e., see column 11). Bergsma et al teach polynucleotide encoding amino

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acid sequence of HUVCT36 set out in FIGS. 1A, 1B and 1c; variants, analogs, derivatives and fragments (refers to the population of receptor variant population of the instant claims). The reference teaches that vectors which include polynucleotides, which encode HUVCT36 and variants, and host cells which are genetically engineered with vectors of the invention and production of polypeptides of the invention by recombinant techniques (refers to 'recombinantly expressed in cells' of the instant claims) (i.e., see column 18). The reference teaches variety expression vectors to be used with the invention (i.e., see column 19). The reference teaches that the vectors generally include selectable markers.

Bergsma et al teach HUVCT36 binding molecules and assays to identify the binding molecules to HUVCT36 (i.e., see columns 29-31). The reference teaches that HUVCT36 receptor expressed in a mammalian or eukaryotic and/or yeast cells and used to screen complex biological mixtures, compound banks, and combinatorial peptide and/or organic libraries for natural and surrogate ligands, which are agonistic, and/or antagonists. In one embodiment the reference teaches that method for screening of peptide libraries for binding partners. Recombinant tagged or labeled HUVCT36 is used to select peptides from a peptide or phosphopeptide library, which interact with HUVCT36. And further the reference teaches one screening procedure includes the use of melanophores (refers to instant claims 'recombinantly expressed in melanophores') which are transfected to express the HUVCT36 of the invention to screen for test compound to observe binding, stimulation and inhibition of the functional aspect (i.e., see column 31).

The claimed invention differs from the prior art teachings by reciting 'dividing said collective receptor variant population into two or more subpopulation and contacting the sub-population with a ligand...' Bergsma et al teach HUVCT36 binding molecules and assays to identify the binding molecules to HUVCT36 (i.e., see columns 29-31). The reference teaches that HUVCT36 receptor expressed in a mammalian or eukaryotic and/or yeast cells and used to screen complex biological mixtures, compound banks, and combinatorial peptide and/or organic libraries for natural and surrogate ligands, which are agonistic and/or antagonists. Bergsma et al do not teach dividing the receptor variant population into sub-populations and detecting the subpopulation which binds to the ligand. It is obvious to one skilled in the art of recombinant technology to do multiple rounds of screening or panning to identify the affinity ligands or specific binding pairs, in panning the phage displaying the ligands which bind to the receptor of interest are further subjected to panning or screening. Hudson et al teach methods for

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production of novel polypeptides with enhanced or modified binding activity or specificity to antigens. The reference teaches recombinant antibody-like molecules (receptor variant population of the instant claims). The reference teaches DNA constructs (phage display libraries) encoding the target-binding polypeptide, selecting a sub-population of display vectors displaying target binding polypeptides (refers to instant claim dividing the population into sub-populations), subjecting the selected sub-populations to one or more cycles of mutagenesis and selection in order to obtain a sub-population of display vectors displaying target binding polypeptides (i.e., see columns 3-5). Thus, it would have been obvious to one skilled in the art at the time the invention was made to use repeated detection steps or serial of screening steps with various sub-populations of the initial library or population. A person skilled in the art would have been motivated to do so because modified or increased affinity ligands would be obtained by the serial screening of the library of ligands.

Applicants traverse the rejection, and argue that all the elements of claimed method for determining binding of a receptor to one or more ligands are not taught or suggested by the cited art. Applicants argue that the cited references alone or in combination fail to teach or suggest contacting receptor variant population with one or more ligands.

Applicant's arguments are not persuasive, because Bergsma et al teach novel human G-protein coupled receptors (refers to the collective receptor variants of the instant claims) and methods of screening of peptide libraries (collective receptor variants) for binding partners (ligands). Bergsma et al do not teach the method step of dividing the receptor variant population. However, in view of combined teachings of Hudson et al and Bergsma et al of record, it would have been obvious to one skilled in the art at the time the invention was made to use repeated detection steps or serial of screening steps with various sub-populations of the initial library or population. A person skilled in the art would have been motivated to do so because modified or increased affinity ligands would be obtained by the serial screening of the library of ligands or

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receptors. Thus, the obviousness rejection of record have been maintained for the reasons set forth in the previous office action mailed on 11/16/04.

Conclusion

14. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Increased Flex Schedule and can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



PADMASHRI PONNALURI
PRIMARY EXAMINER

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

15 September 2005